

### **Amendments to the Claims**

In accordance with 37 CFR 1.121 a Claim Listing is included and the status of each claim is indicated according to the seven permissible status identifiers, i.e. (Original), (Currently Amended), (Cancelled), (Previously Presented), (New), (Not Entered), (Withdrawn). Amended claims use underline for additions and ~~strike through~~ for deletions.

#### **Claim Listing:**

Claim 1. (Currently Amended) A combination therapeutic and diagnostic radiopharmaceutical microparticle comprising a non-radioactive core and at least two different radioactive agents attached to said core by one or more dendritic polymer linking carriers, wherein said core is made from a biocompatible polymer, wherein one of said at least two different radioactive agents is a chelated beta-emitting therapeutic radionuclide that is attached to a first terminal functional group of ~~[[a]]~~ the one or more dendritic polymer linking ~~carrier~~ carriers that is covalently bound to said core, and wherein one of said at least two different radioactive agents is a chelated gamma-emitting diagnostic imaging radionuclide that is attached to a second terminal functional group of ~~[[a]]~~ the one or more dendritic polymer linking ~~carrier~~ carriers that is covalently bound to said core.

Claims 2-7. (Cancelled).

Claim 8. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said therapeutic beta-emitting radionuclide is Yttrium-90.

Claims 9-10. (Cancelled).

Claim 11. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said therapeutic beta-emitting radionuclide is Yttrium-90 and said imaging or diagnostic gamma-emitting radionuclide is selected from the group consisting of indium-111 and Tc-99m.

Claim 12. (Currently Amended) The radiopharmaceutical microparticle of claim ~~particle of claim~~ 1, wherein said radioactive therapeutic agent is bonded to said linking carrier through one or more spacer groups.

Claim 13. (Currently Amended) The radiopharmaceutical microparticle of claim ~~particle of claim~~ 1, wherein said dendritic polymer linking carrier is a poly(amidoamine) dendrimer.

Claim 14. (Currently Amended) The radiopharmaceutical microparticle of claim ~~particle of claim~~ 13, wherein said chelator group is at least one selected from the group consisting of ~~cyclohexyldiethylenetriaminepentaacetic~~ cyclohexyldiethylenetriaminepentaacetic acid ligand (CHX-DTPA), diethylenetriaminepentaacetic acid (DTPA), ethylenediaminetetraacetic acid (EDTA), 1,4,7,10-tetraazacyclododecane-N,- N',N,"N'"tetraacetate (DOTA), tetraazacyclotetradecane-N,N", N"N"-tetraacetic acid (TETA), cyclohexyl 1,2-diamine tetra-acetic acid (CDTA), ethyleneglycol-O,O'-bis(-2-aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N-bis(hydroxybenzyl)-e-thylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic acid (TTHA), hydroxyethylamine triacetic acid (HEDTA), hydroxyethylidene diphosphonate (HEDP), dimercaptosuccinic acid (DMSA), diethylenetriaminetetramethylenephosphonic acid (DTTP) and 1-(p-aminobenzyl)-DTPA, 1,6-diamino hexane-N,N,N',N'-tetraacetic acid, DPDP, and ethylenebis (oxyethylenenitrilo)-tetraacetic acid.

Claim 15. (Previously Presented) The radiopharmaceutical microparticle of claim 13, wherein said therapeutic beta-emitting radionuclide is yttrium-90 and said chelator group is DOTA.

Claim 16. (Cancelled).

Claim 17. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said core comprises a polymer selected from the group consisting of polyacrylate, ethylene-vinyl acetate polymer, an acyl substituted cellulose acetate, polyurethane, polystyrene, polyvinylchloride, polyvinyl flouride, poly(vinyl imidazole), chlorosulphonate polyolefin, polyethylene oxide, blends thereof, and copolymers thereof, a polyphosphazene, a poly(vinyl

alcohol), a polyamide, a polycarbonate, a polyalkylene, a polyacrylamide, a polyalkylene glycol, a polyalkylene oxide, a polyalkylene terephthalate, a polyvinyl ether, a polyvinyl ester, a polyvinyl halide, polyvinylpyrrolidone, a polyglycolide, a polysiloxane, and copolymers thereof, a alkyl cellulose, an hydroxyalkyl cellulose, a cellulose ether, a cellulose ester, and a nitrocellulose.

Claim 18. (Cancelled).

Claim 19. (Cancelled).

Claim 20. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said dendrimer has a disulfide bond in its core.

Claims 21-24. (Cancelled).

Claim 25. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said functional group is at least one selected from the group consisting of ester group, ether group, thiol group, carbonyl group, hydroxyl group, amide group, carboxylic group, and imide group.

Claim 26. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said dendrimers are monodispersed.

Claims 27-28. (Withdrawn).

Claim 29. (Currently Amended) The radiopharmaceutical microparticle of claim 1, wherein said ~~particle~~ microparticle does not leach radionuclide.

Claim 30. (Currently Amended) The radiopharmaceutical microparticle of claim 1, wherein said ~~particle~~ microparticle is spheroidal.

Claim 31. (Currently Amended) The radiopharmaceutical microparticle of claim 1, wherein said

~~particle~~ microparticle has a density in the range of from 1 to 4 gm/cm.<sup>sup.3</sup>.

Claim 32. (Currently Amended) The radiopharmaceutical microparticle of claim 1, wherein said ~~particle~~ microparticle has a density in the range of from 1 to 2 gm/cm.<sup>sup.3</sup>.

Claim 33. (Currently Amended) The radiopharmaceutical microparticle of claim 1, wherein said ~~particle~~ microparticle further comprises a second therapeutic agent or a diagnostic agent.

Claim 34. (Previously Presented) The radiopharmaceutical microparticle of claim 33, wherein said second therapeutic agent or said diagnostic agent is at least one selected from the group consisting of a metal chelate complex, a drug, a prodrug, a radionuclide, a boron addend, a labeling compound, a toxin, a cytokine, a lymphokine, a chemokine, an immunomodulator, a radiosensitizer, an asparaginase, a radioactive halogens, a chemotherapy drug and a contrast agent.

Claim 35. (Currently Amended) A particulate material for radiopharmaceutical use comprising microparticles having: a non-radioactive polymer core ~~made from a biocompatible polymer~~, at least one dendritic polymer linking carrier covalently bound to said core, ~~said dendritic polymer linking carrier having a terminal poly(amidoamine) functional group~~ a first terminal functional group attached for attachment to a first chelated radiopharmaceutical agent and a second functional group attached to a second chelated radiopharmaceutical agent, wherein said first chelated radiopharmaceutical agent selected from the group consisting of a beta emitting therapeutic radionuclide comprising is DOTA-Yttrium-90, and wherein said second chelated radiopharmaceutical agent is a gamma-emitting diagnostic radionuclide selected from the group consisting of DOTA-Indium-111 or DOTA-Technetium-99m ~~wherein said linking carrier comprises a biocompatible polymer~~, and wherein said microparticle has a diameter in the range of from 5 to 200 microns.

Claim 36. (Previously Presented) The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 8-100 microns.

Claim 37. (Previously Presented) The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 25-50 microns.

Claim 38. (Previously Presented) The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 20-30 microns.

Claim 39. (Previously Presented) The particulate material of claim 35, wherein said microparticles have substantially equivalent particle sizes.

Claim 40. (Previously Presented) The particulate material of claim 35, wherein said microparticles are sufficiently large so as to avoid phagocytosis.

Claims 41-71. (Withdrawn).

Claims 72-81. (Cancelled).

Claims 82-84. (Withdrawn).

Claim 85. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said microparticle has a diameter in the range of from about 8 to about 100 microns.

Claim 86. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said microparticle has a diameter in the range of from about 20 to about 30 microns.

Claim 87. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said radioactive therapeutic agent is at least one radionuclide selected from the group consisting of iridium, radium, cesium, phosphorus, yttrium, rhenium, actinium, bismuth, astatine, technetium, indium, iodine, and carbon, nitrogen, fluorine, sodium, magnesium, aluminum, silicon, potassium, vanadium, manganese, gallium, niobium, iodine, lead, Y-90, Bi-213, At-211, I-123, I-125, I-131, Cu-67, Sc-47, Ga-67, Rh-105, Pr-142, Nd-147, Pm-151, Sm-153, Ho-166, Gd-159, Th-161, Eu-152, Er-171, Re-186, Re-188, Tc-99m, In-111, and Tl-201.

Claim 88. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein said chelated radiopharmaceutical agent comprises a first radionuclide and a second radionuclide combined on the same microparticle construct, said first radionuclide comprising a chelated beta-emitting therapeutic radionuclide and said second radionuclide comprising a chelated gamma-emitting diagnostic radionuclide.

Claim 89. (Previously Presented) The radiopharmaceutical microparticle of claim 88, wherein said chelated beta-emitting therapeutic radionuclide comprises Yttrium-90 and said second chelated gamma-emitting diagnostic radionuclide comprises Indium-111 or Technetium-99m.

Claim 90. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein the microparticle is formulated in a pharmaceutical composition in combination with a pharmaceutically acceptable excipient, adjuvant, or carrier.

Claim 91. (Previously Presented) The radiopharmaceutical microparticle of claim 35, wherein the microparticle is formulated in a pharmaceutical composition in combination with a pharmaceutically acceptable excipient, adjuvant, or carrier.

Claim 92. (Previously Presented) The radiopharmaceutical microparticle of claim 1, wherein the microparticle is formulated as a lyophilized preparation.

Claim 93. (Previously Presented) The radiopharmaceutical microparticle of claim 35, wherein the microparticle is formulated as a lyophilized preparation.

Claim 94. (Previously Presented) The radiopharmaceutical microparticle of claim 1, further comprising a spacer group between the dendritic polymer linking carrier and the chelated radiopharmaceutical agent.

Claim 95. (Previously Presented) The radiopharmaceutical microparticle of claim 35, further comprising a spacer group between the dendritic polymer linking carrier and the chelated radiopharmaceutical agent.

Claim 96. (New) The radiopharmaceutical microparticle of claim 1, wherein said dendritic polymer linking carrier is a poly(methyl methacrylate) dendrimer.

Claim 97. (New) A particulate material for radiopharmaceutical use comprising microparticles having: a non-radioactive polymer core made from a biocompatible polymer, a dendritic polymer linking carrier covalently bound to said core, said dendritic polymer linking carrier having a first and a second terminal functional group, a first chelated radiopharmaceutical agent attached to the first terminal functional group of the dendritic polymer linking group, a second chelated radiopharmaceutical agent attached to a second terminal functional group of the dendritic polymer linking group, wherein said first chelated radiopharmaceutical agent is DOTA-Yttrium-90, and wherein said second chelated radiopharmaceutical agent is a gamma-emitting diagnostic radionuclide selected from the group consisting of DOTA-Indium-111 or DOTA-Technetium-99m, wherein said linking carrier comprises a biocompatible polymer, and wherein said microparticle has a diameter in the range of from 5 to 200 microns.

Claim 98. (New) A particulate material for radiopharmaceutical use comprising microparticles having: a non-radioactive polymer core made from a biocompatible polymer, a plurality of dendritic polymer linking carriers covalently bound to said core, said dendritic polymer linking carriers having a terminal functional group, a first chelated radiopharmaceutical agent attached to a terminal functional group of a dendritic polymer linking group, a second chelated radiopharmaceutical agent attached to a terminal functional group of a different dendritic polymer linking group, wherein said first chelated radiopharmaceutical agent is DOTA-Yttrium-90, and wherein said second chelated radiopharmaceutical agent is a gamma-emitting diagnostic radionuclide selected from the group consisting of DOTA-Indium-111 or DOTA-Technetium-99m, wherein said linking carrier comprises a biocompatible polymer, and wherein said microparticle has a diameter in the range of from 5 to 200 microns.

Claim 99. (New) A kit for producing the particulate material for radiopharmaceutical use of claim 1 comprising components A, B, and C:

component A comprising the non-radioactive polymer core as described in claim 1, wherein said core is non-radioactive and is made from a biocompatible polymer, one or more dendritic polymer linking carriers are covalently bound to said core, and said one or more dendritic polymer linking carriers have terminal functional groups;

component B comprising a chelated beta-emitting therapeutic radionuclide as described in claim 1, said chelated beta-emitting therapeutic radionuclide attaching to a first terminal functional group of the one or more dendritic polymer linking carriers that are covalently bound to said core;

component C comprising a chelated gamma-emitting diagnostic imaging radionuclide as described in claim 1, said chelated gamma-emitting diagnostic imaging radionuclide attaching to a second terminal functional group of the one or more dendritic polymer linking carriers that are covalently bound to said core.

Claim 100. (New) The radiopharmaceutical microparticle as in any one of claims of claim 97, 98, and 99, wherein said chelator group is at least one selected from the group consisting of cyclohexyldiethylenetriaminepentaacetic acid ligand (CHX-DTPA), diethylenetriaminepentaacetic acid (DTPA), ethylenediaminetetraacetic acid (EDTA), 1,4,7,10-tetraazacyclododecane-N,- N',N,"N""tetraacetate (DOTA), tetraazacyclotetradecane-N,N", N"N"-tetraacetic acid (TETA), cyclohexyl 1,2-diamine tetra-acetic acid (CDTA), ethyleneglycol-O,O'-bis(-2-aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N-bis(hydroxybenzyl)-e-thylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic acid (TTHA), hydroxyethylidiamine triacetic acid (HEDTA), hydroxyethylidene diphosphonate (HEDP), dimercaptosuccinic acid (DMSA), diethylenetriaminetetramethylenephosphonic acid (DTTP) and 1-(p-aminobenzyl)-DTPA, 1,6-diamino hexane-N,N,N',N'-tetraacetic acid, DPDP, and ethylenebis (oxyethylenenitrilo)-tetraacetic acid.

Claim 102. (New) The radiopharmaceutical microparticle as in any one of claims of claim 97, 98, and 99, wherein said core comprises a polymer selected from the group consisting of polyacrylate, ethylene-vinyl acetate polymer, an acyl substituted cellulose acetate, polyurethane,



polystyrene, polyvinylchloride, polyvinyl flouride, poly(vinyl imidazole), chlorosulphonate polyolefin, polyethylene oxide, blends thereof, and copolymers thereof, a polyphosphazine, a poly(vinyl alcohol), a polyamide, a polycarbonate, a polyalkylene, a polyacrylamide, a polyalkylene glycol, a polyalkylene oxide, a polyalkylene terephthalate, a polyvinyl ether, a polyvinyl ester, a polyvinyl halide, polyvinylpyrrolidone, a polyglycolide, a polysiloxane, and copolymers thereof, a alkyl cellulose, an hydroxyalkyl cellulose, a cellulose ether, a cellulose ester, and a nitrocellulose.

Claim 103. (New) The radiopharmaceutical microparticle as in any one of claims of claim 97, 98, and 99, wherein said functional group is at least one selected from the group consisting of ester group, ether group, thiol group, carbonyl group, hydroxyl group, amide group, carboxylic group, and imide group.